UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

VB

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/127,138	07/31/98	GRUENBERG	M	24731-500E

HM22/0515

STEPHANIE SEIDMAN
HELLER EHRMAN WHITE & MCAULIFFE
4250 EXECUTIVE SQUARE,
7TH FLOOR
LA JOLLA CA 92037

EXAMINER	
SCHWADRON,R	
ART UNIT	**PAPER NUMBER**
1644	14

DATE MAILED: 05/15/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/127,138	Applicant(s) Gruenberg
	Examiner Ron Schwadron, Ph.D.	Group Art Unit 1644

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *18-21, 46-54, 68-71, 73-135, and 153* is/are pending in the application.

Of the above, claim(s) *18-21, 46, 47, 49, 50, 52-54, 68-71, 73-123, 125,* 128-135, 153 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *48, 51, 124, 126, and 127* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. Applicant's election without traverse of Group VIII and the species Th1 in Paper No. 12 is acknowledged.

2. Claims 49,125,128-130,18-21,46,47,50,52-54,68-71,73-123,131-135,153 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions or species. Election was made **without** traverse in Paper No. 12.

3. Claims 48,51,124,126,127 are under consideration. Regarding claim 125, while said claim was erroneously included in Group VIII, it actually depends on claim 18 and should have been included in Group I. Regarding claim 127, said claim, while depending on cancelled claim 16 was erroneously included in Group VIII. For the purposes of this Office Action the claim will be examined in the context of the invention of Group VIII (eg. as if it depended on claim 48). Applicant needs to amend said claim so that it depends on claim 48.

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because of the following reasons. There were two different defective declarations filed with the instant application. The first declaration is defective because it is unsigned and because it claims priority to itself under 35 USC 120. The second declaration is defective because it does not correctly identify the provisional application to which applicant claims priority and it does not list the application number of the PCT to which priority under U.S.C. 120 is desired.

5. Regarding the priority data disclosed in the specification, page 1, second paragraph, the address of applicants' attorney's law firm was erroneously placed in the middle of a sentence related to the priority claim to PCT/US96/12170.This information should be deleted.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 48,51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabling for the claimed method wherein regulatory immune cells per se are generated. The specification discloses the claimed methods wherein T cells/T cell subsets are generated. However, regulatory immune cells encompasses nonT cells such as dendritic cells, macrophages, NK cells, etc. There is no evidence of record that such cells can be generated using the claimed method. For example, macrophages and dendritic cells are not CD3 or CD2 positive, and therefore said cells could not be grown using the method disclosed in the specification which requires use of a CD3 or CD2 stimulating agent. There is no disclosure or guidance in the specification as to how the claimed method could be used to grow dendritic cells, macrophages, NK cells, etc. For example, Steinman et al. (US Patent 5,994,126) discloses that specific reagents not recited in the claims or disclosed in the specification are required to grow/generate dendritic cells (eg. see claims). There is no guidance in the specification as how the claimed method could be used for the growth of dendritic cells, macrophages or other immune cells that are not of the T cell lineage. Therefore, the specification is not enabling for the instant invention.

8. Claims 48 and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the recitation of "mammal" in claim 48. There is no disclosure of the method of claim 48 which recites mammal in the specification as originally filed. There is no support in the specification as originally filed for the scope of the claimed invention (eg. the claimed invention constitutes new matter).

9. Claims 48,51,124,126,127 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 48 and 124 are indefinite in the recitation of "regulatory immune cells" or "regulatory T cells" because it is unclear what these phrases mean or encompass. The specification on page 19 discloses that "a regulatory immune cell is any mononuclear cell with a defined cytokine production profile in which such cytokine profile does not directly mediate an effector function" and that said cell "has the ability to control or direct an immune response, but does not act as an effector cell in the response". However, it is unclear what this means or encompasses. While the specification discloses that Th1 or Th2 are "regulatory immune cells", the art recognizes that said cells are effector cells with regards to the pathogenesis of a variety of different autoimmune diseases (see Liblau et al., pages 34-38). For example, Liblau et al. teach that Th1 cells are involved in the pathogenesis of IDDM wherein said cells bind islet antigens via TCR mediated antigen specific recognition of said islet antigens (see page 35, first column penultimate paragraph). Liblau et al. teach that the lymphokines secreted by said cells are involved in the pathogenesis of IDDM. The art recognizes that virtually all secreted lymphokines have some sort of effector function. For example, Mosmann et al. (Immunology Today, 1996) teach that Th1 (a form of regulatory cell as defined in the specification) secrete lymphotoxin (see Table 1), wherein the art recognizes that lymphotoxin is directly cytotoxic to viruses and tumor cells (see Arai et al., columns 1 and 2). Thus, said Th1 can directly eliminate pathogens or tumor cells via secretion of lymphotoxin. Thus, according to the definition in the specification Th1, Th2 or Th3 are not "regulatory immune cells" because they function as effector cells and the cytokines they produce also function in a variety of different effector mechanisms. It is unclear as to what cell population is encompassed by this term and it is unclear what the aforementioned definition actually means.

Claim 48 is indefinite in the recitation of "alter the in vivo regulatory immune cell balance" and claim 124 is indefinite in the recitation of "altering the regulatory balance of immune cell ", because it is unclear what these phrases mean or encompass. For example, is the altering in relation to a population seen in normal or disease patients. It is also unclear as to what would constitute an "altering" (eg. is this a functional parameter or refer just to numbers of cells). If the aforementioned refers to number of cells, what is the quantitative change which

reflects a state of alteration . If the aforementioned refers to a functional property, then what is this property and how is it determined. For the reason mentioned in the previous paragraph it is also unclear as to what "regulatory" immune cells means or encompasses.

10. Regarding priority for the claimed inventions with regards to the application of prior art, the claimed inventions are not disclosed in parent application provisional application 60/044693 (the application formerly known as 08/506668), and therefore priority with regards to the application of prior art is taken as the filing date of parent application 08/700565 to which applicant claims priority.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

12. Claims 48,51,124,127 are rejected under 35 U.S.C. 102(e) as being anticipated by Babbitt et al. (US Patent 5,766,920).

While it is unclear what the terms referred to in paragraph 9 of this Office Action mean or encompass, for the purposes of application of prior art the claimed methods will be interpreted as methods wherein Th1 cells are expanded and subsequently administered. Babbitt et al. teach methods for producing Th1 cells, wherein patient mononuclear cells are removed and expanded in vitro (see columns 5 and 6). The method taught by Babbitt et al. uses IFN γ enriched supernatants and OKT3 (eg. antiCD3 antibody) to produce Th1 populations (see columns 5 and 6). Babbitt et al. teach that autologous expanded Th1 cells are reinfused to treat autoimmune disease (see column 2, first complete paragraph). The cells are expanded to clinically relevant numbers (see column 19).

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness

rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 48,51,124,126,127 are rejected under 35 U.S.C. 103(a) as being unpatentable over Babbitt et al. (US Patent 5,766,920).

While it is unclear what the terms referred to in paragraph 9 of this Office Action mean or encompass, for the purposes of application of prior art the claimed methods will be interpreted as methods wherein Th1 cells are expanded and subsequently administered. Babbitt et al. teach methods for producing Th1 cells, wherein patient mononuclear cells are removed and expanded in vitro (see columns 5 and 6). The method taught by Babbitt et al. uses IFN γ enriched supernatants and OKT3 (eg. antiCD3 antibody) to produce Th1 populations (see columns 5 and 6). Babbitt et al. teach that autologous expanded Th1 cells are reinfused to treat autoimmune disease (see column 2, first complete paragraph). The cells are expanded to clinically relevant numbers (see column 19). Babbitt et al. do not teach that at least 10^{10} cells were administered. Babbitt et al. teach that approximately 10^9 cells are administered in a particular patient (see column 19). A routineer would have administered more or less cells depending on the particular patient and disease to be treated. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Babbitt et al. teach the claimed method wherein approximately 10^9 cells are administered in a particular patient and a routineer would have administered more or less cells depending on the particular patient and disease to be treated.

15. No claim is allowed.

16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 308-4242.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644